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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,422	11/07/2006	Eggert Stockfleth	50125/084002	7550

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
MI, QIUWEN	
ART UNIT	PAPER NUMBER
1655	

NOTIFICATION DATE	DELIVERY MODE
12/18/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/574,422	STOCKFLETH, EGGERT	
	Examiner	Art Unit	
	Qiuwen Mi	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 3-6, and 8-35* is/are pending in the application.

4a) Of the above claim(s) *33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8-32 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/9/2007, 12/3/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment in the reply filed on 10/9/07 is acknowledged. Any rejection that is not reiterated is hereby withdrawn.

Claims Pending

Claims 1, 3-6, and 8-35 are pending. Claims 2 and 7 are cancelled. Claims 33 and 34 are withdrawn. Claims 1, 3-6, 8-32, and 35 are examined on the merits.

Claim Rejections –35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, 8-20, 27, and 29 are rejected under 35 USC § 102 (a) as being anticipated by Li et al [The Chemopreventive Effects of Tea on Human Oral Precancerous Mucosa Lesions, Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N.Y.), (1999 Apr) Vol. 220, No. 4, pp. 218-24)], as evidenced by Dou et al (US 2002/0151582)*.

This is a new rejection necessitated by the Applicant's amendment filed on 10/9/07.

Li et al teach administering tea orally and topically to human with oral precancerous mucosa lesions, and the size of oral lesion was decreased in 37.9% of patients (see Title, Abstract). Li et al also teach that tea was composed of a dried mixture of the whole water extract of green tea, green tea polyphenols (40%), and tea pigments in the ratio of 4:1: 1, and patients were painted on the lesions topically with mixed tea in glycerin (additive) at the concentration of 10% (page 219, left column, 3rd paragraph).

As evidenced by Dou et al (US 2002/0151582), green tea contains polyphenol compounds EGCG (formula I and II in claims 13 and 14 are thus met), ECG, GCG, or CG (claim 3).

Therefore, the reference is deemed to anticipate the instant claim above.

Claims 1, 3-6, and 8-20 are rejected under 35 USC § 102 (b) as being anticipated by Jia et al (Effects of Tea on Preneoplastic Lesions and Cell Cycle Regulators in Rat Liver, Cancer Epidemiology, Biomarkers & Prevention (2002) 11: 1663-1667).

This is a new rejection necessitated by the Applicant's amendment filed on 10/9/07.

Jia et al teach the effects of tea polyphenols and tea pigments on rat liver precancerous lesion, and the results suggest that tea polyphenols and tea pigments are effective in preventing the precancerous liver lesions in rats (see Title, Abstract). Jia et al also teach that the purity of tea polyphenols was 40%, and it is composed mainly of polyphenolic compounds EGCG (13%) (thus formula I and II in claims 13 and 14 are met), (-) epicatechin (3%), (-) epicatechin gallate (6%), and epigallocatechin (6%) (page 1663, right column, last paragraph).

Therefore, the reference is deemed to anticipate the instant claim above.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 8-27, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al [The Chemopreventive Effects of Tea on Human Oral Precancerous Mucosa Lesions, Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N.Y.), (1999 Apr) Vol. 220, No. 4, pp. 218-24)], as evidenced by Dou et al (US 2002/0151582)*.

This is a new rejection necessitated by the Applicant's amendment filed on 10/9/07.

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As evidenced by Dou et al (US 2002/0151582), green tea contains polyphenol compounds EGCG (formula I and II in claims 13 and 14 are thus met), ECG, GCG, or CG (claim 3).

Li et al do not teach the amount of the polyphenols in the composition.

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the inventions of Li et al since they provide scientific data for human oral precancerous mucosa lesions, one of ordinary skill in the art would have been motivated to make the modifications. The result-effective adjustment in conventional working parameters (e.g., determining an appropriate amount of the each polyphenol components as claimed isolated from green tea within the composition) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Claims 1, 3-6, and 8-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jia et al (Effects of Tea on Preneoplastic Lesions and Cell Cycle Regulators in Rat Liver, Cancer Epidemiology, Biomarkers & Prevention (2002) 11: 1663-1667).

This is a new rejection necessitated by the Applicant's amendment filed on 10/9/07.

Jia et al teach the effects of tea polyphenols and tea pigments on rat liver precancerous lesion, and the results suggest that tea polyphenols and tea pigments are effective in preventing the precancerous liver lesions in rats (see Title, Abstract). Jia et al also teach that the purity of tea polyphenols was 40%, and it is composed mainly of polyphenolic compounds EGCG (13%) (thus formula I and II in claims 13 and 14 are met), (-) epicatechin (3%), (-) epicatechin gallate (6%), and epigallocatechin (6%) (page 1663, right column, last paragraph).

Jia et al do not teach the amount of the polyphenols in the composition.

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the inventions of Jia et al since it provides scientific data for treating rat liver precancerous lesion, one of ordinary skill in the art would have been motivated to make the modifications. The result-effective adjustment in conventional working parameters (e.g., determining an appropriate amount of the each polyphenol components as claimed isolated from green tea within the composition) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Claims 1, 3-6, 8-32, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al [The Chemopreventive Effects of Tea on Human Oral Precancerous Mucosa

Lesions, Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N.Y.), (1999 Apr) Vol. 220, No. 4, pp. 218-24)], in view of Brash et al (US 2002/0198161), and further in view of Voet (US 6,723,750), as evidenced by Dou et al (US 2002/0151582)*.

This is a new rejection necessitated by the Applicant's amendment filed on 10/9/07.

Li et al teach administering tea orally and topically to human with oral precancerous mucosa lesions, and the size of oral lesion was decreased in 37.9% of patients (see Title, Abstract). Li et al also teach that tea was composed of a dried mixture of the whole water extract of green tea, green tea polyphenols (40%), and tea pigments in the ratio of 4:1: 1, and patients were painted on the lesions topically with mixed tea in glycerin (additive) at the concentration of 10% (page 219, left column, 3rd paragraph).

As evidenced by Dou et al (US 2002/0151582), green tea contains polyphenol compounds EGCG (formula I and II in claims 13 and 14 are thus met), ECG, GCG, or CG (claim 3).

Li et al do not teach additive isopropyl myristate, form of ointment, or combined with a different treatment curettage, or the claimed amount of the polyphenols.

Brash et al teaches that skin precancers are being treated, the preferred mode of administration is topical. The topical application may contain carrier, excipient or vehicle ingredients such as isopropyl myristate etc., and mixtures thereof to form lotions, creams, emulsions, gels, or ointments [0086].

Voet teaches that the current management options for visible or easily perceived and diagnosed precancerous dermatological lesions such as Aks (thus claim 35 is met) include cryosurgery with liquid nitrogen, topical treatment, and curettage (col 2, lines 15-20). Voet also teaches that curettage, which involves the use of a curette to scrape away the lesion, is another common method of treatment for easily perceptible precancerous skin lesions. The primary advantage of curettage is the ability to submit the specimen for histologic analysis.

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the carrier isopropyl myristate and ointment form of Brash et al, and the treatment of curettage from Voet in the current invention since carrier isopropyl myristate and ointment form are the conventional carrier and pharmaceutical form that have been used successfully in treating precancerous lesions in the topical route according to Brash et al; and combining the treatment curettage from Voet with the topical could monitor the histologic status of the tissue treated by topical administration. Since both Brash et al, and the treatment of curettage from Voet yielded beneficial results in treating precancerous lesions, one of ordinary skill in the art would have been motivated to make the modifications. The result-effective adjustment in conventional working parameters (e.g., determining an appropriate amount of the each polyphenol components as claimed isolated from green tea within the composition) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Claims 1, 3-6, 8-28, 30-32, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jia et al (Effects of Tea on Preneoplastic Lesions and Cell Cycle Regulators in Rat Liver, Cancer Epidemiology, Biomarkers & Prevention (2002) 11: 1663-1667), and further in view of Voet (US 6,723,750), as evidenced by Dou et al (US 2002/0151582)*.

This is a new rejection necessitated by the Applicant's amendment filed on 10/9/07.

Jia et al teach the effects of tea polyphenols and tea pigments on rat liver precancerous lesion, and the results suggest that tea polyphenols and tea pigments are effective in preventing the precancerous liver lesions in rats (see Title, Abstract). Jia et al also teach that the purity of tea polyphenols was 40%, and it is composed mainly of polyphenolic compounds EGCG (13%) (thus formula I and II in claims 13 and 14 are met), (-) epicatechin (3%), (-) epicatechin gallate (6%), and epigallocatechin (6%) (page 1663, right column, last paragraph).

Jia et al do not teach additive isopropyl myristate, form of ointment, or combined with a different treatment curettage, or the claimed amount of the polyphenols.

Brash et al teaches that skin precancers are being treated, the preferred mode of administration is topical. The topical application may contain carrier, excipient or vehicle

ingredients such as isopropyl myristate etc., and mixtures thereof to form lotions, creams, emulsions, gels, or ointments [0086].

Voet teaches that the current management options for visible or easily perceived and diagnosed precancerous dermatological lesions such as Aks (thus claim 35 is met) include cryosurgery with liquid nitrogen, topical treatment, and curettage (col 2, lines 15-20). Voet also teaches that curettage, which involves the use of a curette to scrape away the lesion, is another common method of treatment for easily perceptible precancerous skin lesions. The primary advantage of curettage is the ability to submit the specimen for histologic analysis.

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the carrier isopropyl myristate and ointment form of Brash et al, and the treatment of curettage from Voet in the current invention since carrier isopropyl myristate and ointment form are the conventional carrier and pharmaceutical form that have been used successfully in treating precancerous lesions in the topical route according to Brash et al; and combining the treatment curettage from Voet with the topical could monitor the histologic status of the tissue treated by topical administration. Since both Brash et al, and the treatment of curettage from Voet yielded beneficial results in treating precancerous lesions, one of ordinary skill in the art would have been motivated to make the modifications. The result-effective adjustment in conventional working parameters (e.g., determining an appropriate amount of the each polyphenol components as claimed isolated from green tea within the

composition) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

*This reference is cited merely to relay an intrinsic property and is not used in the basis for rejection *per se*.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Qiuwen Mi

TERRY MCKELVEY, PH.D.
SUPERVISORY PATENT EXAMINER